Three-dimensional bioprinted glioblastoma microenvironments model cellular dependencies and immune interactions.

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Public Summary:
To better study glioblastomas in the lab, we create a 3D cancer model that also contains immune cells, and showed that this model is more predictivie of patient survival.

Scientific Abstract:
Brain tumors are dynamic complex ecosystems with multiple cell types. To model the brain tumor microenvironment in a reproducible and scalable system, we developed a rapid three-dimensional (3D) bioprinting method to construct clinically relevant biomimetic tissue models. In recurrent glioblastoma, macrophages/microglia prominently contribute to the tumor mass. To parse the function of macrophages in 3D, we compared the growth of glioblastoma stem cells (GSCs) alone or with astrocytes and neural precursor cells in a hyaluronic acid-rich hydrogel, with or without macrophage. Bioprinted constructs integrating macrophage recapitulate patient-derived transcriptional profiles predictive of patient survival, maintenance of stemness, invasion, and drug resistance. Whole-genome CRISPR screening with bioprinted complex systems identified unique molecular dependencies in GSCs, relative to sphere culture. Multicellular bioprinted models serve as a scalable and physiologic platform to interrogate drug sensitivity, cellular crosstalk, invasion, context-specific functional dependencies, as well as immunologic interactions in a species-matched neural environment.